

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
9 September 2005 (09.09.2005)

PCT

(10) International Publication Number
WO 2005/082859 A1

(51) International Patent Classification⁷: **C07D 223/16**,
401/12, 417/12, 413/12, 403/12, 409/12, 405/12, 413/14,
417/06, 403/06, A61K 31/55, A61P 25/22, 25/24, 25/30,
3/04

(21) International Application Number:
PCT/US2005/005418

(22) International Filing Date: 18 February 2005 (18.02.2005)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/547,681 25 February 2004 (25.02.2004) US

(71) Applicant (for all designated States except US): **ELI LILLY AND COMPANY** [US/US]; Lilly Corporate Center, Indianapolis, IN 46285 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **ALLEN, John, Gordon** [US/US]; 5886 North Delaware Street, Indianapolis, Indiana 46220 (US). **BRINER, Karin** [CH/US]; 7649 Pinesprings East Drive, Indianapolis, Indiana 46256 (US). **COHEN, Michael, Philip** [US/US]; 8141 Bowline Court, Indianapolis, Indiana 46236 (US). **GALKA, Christopher, Stanley** [US/US]; 13690 N. Stone Have Drive, Carmel, Indiana 46033 (US). **HELLMAN, Sarah, Lynne** [US/US]; 7620 Kimcoe Lane, Indianapolis, Indiana 46254 (US). **MARTINEZ-GRAU, Marla, Angeles** [ES/ES]; Lilly S. A., Avenida de la Industria 30, E-28108 Alcobendas (Madrid) (ES). **REINHARD, Matthew, Robert** [US/US]; 8301 Scarsdale Court, Indianapolis, IN 46256 (US). **RODRIGUEZ, Michael, John** [US/US]; 7649 Gordonshire Court, Indianapolis, Indiana 46278 (US). **ROTHHAAR, Roger, Ryan** [US/US]; 5282 West 775 South, Reelsville, In 46171 (US). **TIDWELL, Michael, Wade** [US/US]; 665 Downing Drive, Greenwood, Indiana 46143 (US). **VICTOR, Frantz** [US/US]; 4855 North Tuxedo Street, Indianapolis, Indiana 46205 (US). **WILLIAMS, Andrew, Caerwyn** [GB/GB]; Eli Lilly and Company Limited, Kingsclere Road, Basingstoke Hampshire RG21 6XA (GB). **ZHANG, Deyi** [US/US]; 1372 Kirklees Drive, Carmel, Indiana 46032 (US). **BOYD, Steven, Armen**

[US/US]; 5665 Saint Vrain Road, Longmont, Colorado 80503-9061 (US). **CONWAY, Richard, Gerard** [US/US]; 3315 Beech Drive, Carmel, Indiana 46033 (US). **DEO, Arundhati, S.** [US/US]; 2342 Hillside Avenue, Saint Paul, Minnesota 55108 (US). **LEE, Wai-Man** [CN/US]; 2128 24th Avenue, Longmont, Colorado 80501 (US). **SIEDEM, Christopher, Stephen** [US/US]; 4215 Redmond Drive, Longmont, Colorado 80503 (US). **SINGH, Ajay** [IN/US]; 2028 South Evanston Court, Aurora, Colorado 80014 (US).

(74) Agents: **TUCKER, R., Craig et al.**; P. O. Box 6288, Indianapolis, Indiana 46206-6288 (US).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

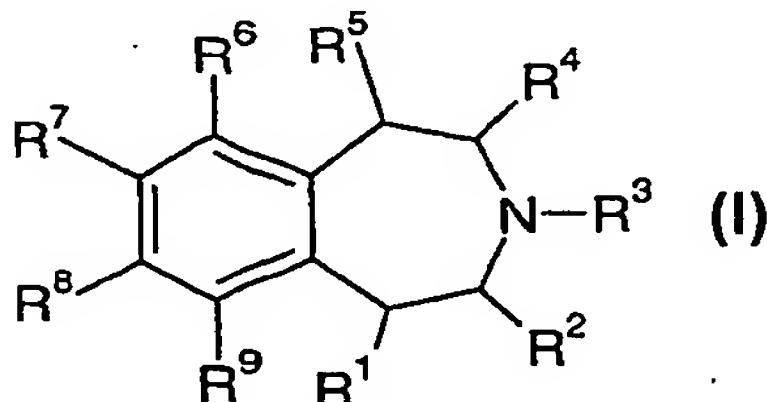
(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Declarations under Rule 4.17:

— as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii)) for the following designations AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA,

[Continued on next page]

(54) Title: 6-SUBSTITUTED 2,3,4,5-TETRAHYDRO-1H-BENZO[D]AZEPINES AS 5-HT_{2C} RECEPTOR AGONISTS



(57) Abstract: The present invention provides 6-substituted 2,3,4,5-tetrahydro-1H-benzo[d]azepines of Formula I as selective 5-HT_{2C} receptor agonists for the treatment of 5-HT_{2C} associated disorders including obesity, obsessive/compulsive disorder, depression, and anxiety: I where: R₆ is -C≡C-R₁₀, -O-R₁₂, -S-R₁₄, or -NR₂₄R₂₅; and other substituents are as defined in the specification.



ZM, ZW, ARIPO patent (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG)

- as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii)) for the following designations AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,

TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, ARIPO patent (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG)

Published:

- with international search report

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.